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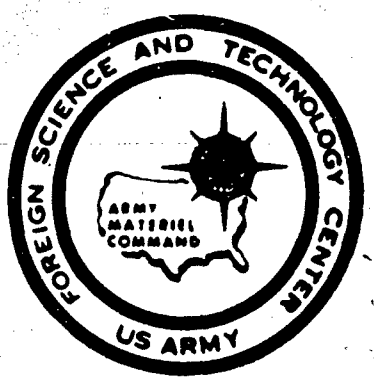

DYNAMICS OF A PLASMACYTIC REACTION WHEN TETANUS ANTITOXIN IS INTRODUCED BY AEROSOL AND SUBCUTANEOUSLY

by

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13. ABSTRACT

The author tested the efficacy of tetanus antitoxin given subcutaneously and by aerosol. The antitoxin was administered alone and with an adjuvant of typhoid fever antigen. Results are compared with those of the fever antigens alone. Comparisons are made between reactions of local lymph nodes and those remote from the place of antitoxin introduction.

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Tetanus						
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Tetanus antitoxin						
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Typhoid fever antigen						
Inguinal lymph nodes						
Neck lymph nodes						

TECHNICAL TRANSLATION

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NOTICE

In the opinion of a number of researchers, a plasmacytic reaction can serve as an indicator of immunobiological alteration in an organism when vaccination is used against various infections. The intensity of proliferation of the immunizing cells depends on the dosage, the nature and the physical condition of the antigens, and also on the place and method of their entrance into the organism (Fagraeus, 1948, Coons et al., 1955; Gurvich and Shumakova, 1958; Zdrodovskiy, 1961; Fontalin, 1967).

The present investigation embraces the study of the dynamics and intensity of the plasmacytic reaction when tetanus antitoxin is provided by aerosol and subcutaneously. The aerosol tetanus antitoxin was used alone or mixed with salmonella type antigens, used by us an an adjuvant. The dosage of tetanus antitoxin inhaled by a rabbit amounted to 15-20 EC, while the salmonella antigens amounted to 0.8-1 mg. For subcutaneous absorptive injection we used tetanus antitoxin in a 10 EC dosage.

Rabbits were sacrificed on the first, seventh, fifteenth and thirtieth days after one immunization and on the second, sixth, twelfth and thirthieth days after repeated injection, carried out at intervals of 30 days. The plasmacytic reaction was studied by computing the number of immature cells of a plasmatic type in the smear prints from the lymph nodes by the method described by Pokrovskoy and Kaganovoy (1947), Gurvich and Shumakovoy (1958). The cytological investigation of the smear prints, which required two to four rabbits each day, was carried out with a microscope at a magnification of 945. The results of counting the cells were worked out statistically.

When immunization was provided by aerosol, the polydispersion of the preparation and its precipitation throughout the respiratory tract was considered, and the tracheal tubes and the lymph nodes in the neck were examined as a means of control. When the antitoxin was introduced subcutaneously into the thigh of the right leg, the first inguinal was taken as the lymphatic node control.

After a single exposure to an aerosol with dry tetanus antitoxin, proliferation of the plasmatic cells was notriced at least in the control lymph glands on the seventh and fifteenth days; at the same time, in a distanct inguinal node no tendency toward an increased number of plasmatic cells (Figure 1) was found. The plasmocytic reaction picture changed after a second exposure to tetanus antitoxin with the aerosol method. Thus, the cell reaction went on in the generalized way and was checked, not only in the regional, but also in the distant (inguinal) lymphatic nodes. The proliferation of the cells began as early as the second day and was characterized by the following mean geometrical indicators: tracheal tubes----80:1.2, neck--53:1.03, inguinal--62:1.2 cells. In all lymphatic nodes investigated, the maximum number of plasmatic cells was found on the tenth to twelfth days. This was much more intensively expressed in the tracheal and neck nodes than in the inguinal node. By the thirtieth day the number of plasmatic cells had been reduced in all lymphatic nodes. According to our observations the plasmocytic reaction in the animals infected subcutaneously with absorptive tetanus antitoxin progressed similarly (see Figure 1). After a single introduction of antitoxin, insignificant increases in the plasmacytic cells were observed by the seventh day, only in the regional right inguinal node. Repeated subcutaneous injection of the adsorptive antitentanus toxin was expressed, as in a second introduction of tetanus antitoxin by the aerosol method, by a generalized plasmocytic reaction, where the reaction occurred a little later in the distant lymphatic nodes than in the regional ones. Thus, in two days after a second immunization the number of cells in the right inguinal node increased to 89 × 1.47; it was less in the distant lymphatic nodes for the same period of time. After six days we counted 108 × 1.1 cells in the right inguinal node, 50 × 1.08 in the left one, and 23 × 1.25 in the tracheal node. The maximum accumulation of cells of a plasmacytic type was found in all lymphatic nodes investigaed on the tenth to twelfth day. In addition, the number of cells in the different nodes was as follows: in the right inguinal 139 × 1.14, in the left inguinal 88 × × 1.02, in the tracheal 78 × 1. By the 30th day the number of plasmacytic cells had dropped to normal in the lymphatic nodes distant from the place of introduction and was higher in the regional node.

In immunizing rabbits with a mixture of tetanus antitoxin and typhoid fever antigens by the aerosol method, the proliferation of cells and apparent after just a singel introduction of the preparation, not only in the regional, but also in the distant, lymphatic nodes (Figure 2). On the fifteenth day the cellular reaction was maximum: the number of cells in the tracheal node was 129 × 1.07 and in the neck node was

116 × 1.07. In distant lymphatic nodes the plasmacytic reaction came later than in the regional ones, and was less pronounced. By the thirtieth day the number of cells in all nodes was reduced, but in the tracheal and neck nodes the reaction continued at a high level (106 × × 1.1 and 97 × 1.1, respectively).

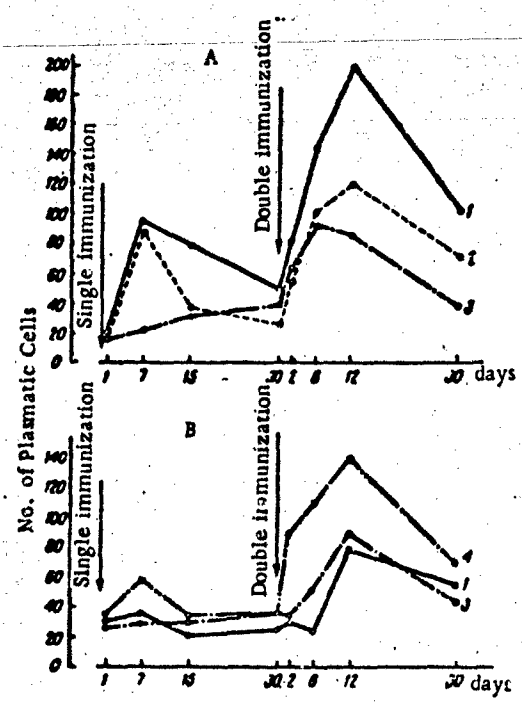

Figure 1. Dynamics of Plasmacytic Reaction with Aerosol Immunization of Tetanus Antitoxin (a) and with Subcutaneous Immunization of Adsorptive Tetanus Antitoxin (b).
Key: 1, Tracheal; 2, Neck; 3, Inguinal left; 4, Inguinal right lymphatic node.

Repeated introduction of tetanus antitoxin with typhoid fever antigen caused a sharp proliferation of cells of a plasmatic type. For six days the number of cells increased significantly in all lymphatic nodes investigated, the reached a maximum on the twelfth day. By the thirtieth day the number of plasmatic cells had dropped, but the plasmatic reaction in this period was more pronounced than after immunization by tetanus antitoxin alone, independent of the method of its introduction (see Table).

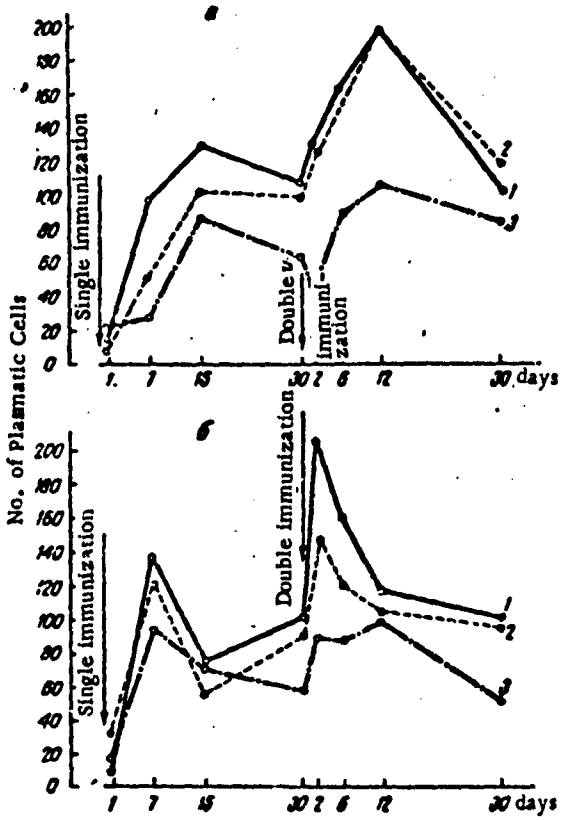

Figure 2. Dynamics of Plasmacytic Reaction with Aerosol Immunization of Tetanus Antitoxin in Combination with Typhoid Fever Antigen (a) and with Typhoid Fever Antigen Alone (b).
Key: 1, Tracheal; 2, Neck; 3, Inguinal Lymphatic Node.

The plasmacytic reaction after single and double immunization by aerosol tetanus antitoxin combined with typhoid fever antigen proceeded just as after introduction of typhoid fever antigen by aerosol (Aleksandrov et al., 1964). Both single and double introductions by aerosol of typhoid fever antigen and typhoid fever antigen along with tetanus antitoxin were accompanied by the development of generalized plasmatic cell reaction.

TABLE. TITERS OF ANTITOXIN IN RABBITS AT VARIOUS PERIODS AFTER SECOND IMMUNIZATION.

Method	Vaccination	Titers of antitoxin (in AE/ma)				
		Until immunization	After second immunization			
			For two days	For six days	For 12 days	For 30 days
By aerosol	Tetanus antitoxin	<0,001 <0,001 <0,001	0,001 0,05 <0,001	0,5 0,5 0,1 1	1 2 0,1	0,1 0,01
	Tetanus antitoxin + typhoid fever antigen	<0,001 <0,001 <0,001	>0,1<0,5 >0,1<0,5	1 >3<5 1	5 >1<5 >1<5	0,5 >0,1<0,5
Subcutaneous	Adsorptive tetanus antitoxin	<0,001 <0,001 <0,001	>1<5 1 >0,1<1	1 3 5 >5<10	>1<3 >3<5	>1<5 >1<5

Barr (1959), Kind and Johnson (1959), Ward et al., (1959), Lan(ge)-voort et al., (1963), Gurvich et al., (1964), Munoz (1961), A(-)tikyan (1966), Frolova (1966), associate the adjuvant action of the gram negative staining of bacteria with subcutaneous injection with their stimulating influence on the reticulo-endothelial system, leading to proliferation and differentiation of lymphoid cells and aggravation/intensification of the synthesis [illegible].

It is possible to presume that one of the mechanisms of the adjuvant activity of the typhoid fever antigen with the aerosol method of introduction with antitoxins, just as with the subcutaneous method, is stimulization of the plasmacellular reaction. The results found agree with the given immunized investigations in these rabbits: the level of antitoxin in the blood [illegible] and intensiveness of plasmacytic reaction were higher in animals [illegible], in addition to tetanus antitoxin, typhoid fever antigens.

In this way, combining tetanus antitoxin with typhoid fever antigens with aerosol immunization, it is possible to increase the immunizing response on the part of the organism by including the split line of lymph nodes in the immunogensis.

Conclusions

1. Immunization against tetanus by aerosol was accompanied by a development of plasmacytic reaction in the lymphoid of the vaccinated rabbits, as evidenced by immunological structure of the organism.

2. After a single immunization by aerosol tetanus antitoxin, proliferation of the immunizing cells of a plasmatic type were observed only in the lymphatic nodes local to the place of introduction (tracheal and neck), and a second introduction of antitoxin with the same method was accompanied by the development of generalized plasmacytic reaction.

3. The dynamics and intensity of the plasmacytic reaction were identical with aerosol and subcutaneous introduction of the tetanus antitoxin.

4. With a combined immunization of aerosol of tentanus antitoxin and typhoid fever antigen, just as with immunization of the typhoid fever antigen by aerosol alone, the plasmacytic reaction led to a generalized nature and developed in lymph glands, both local and remote from the place of introduction, right after a single application of antigens.

5. One of the mechanisms of adjuvant activity of typhoid fever antigen on the formation of antitoxin immunity to tetanus with aerosol immunization and with subcutaneous immunization is the stimulation of a plasmacellular reaction in a split line of the lymphatic nodes.

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